II. Remarks

A. Status of the Claims

Reconsideration and allowance of the subject application are respectfully requested. Claims 1, 2, 5-7, 9, 10-12 and 69-71 are currently pending. Claim 1 is independent. Claim 1 has been amended to address an antecedent basis issue and to recite that the analyzer is a subtraction analyzer. Support for the subtraction analyzer limitation may be found in paragraphs [0093] and [0094] and generally throughout the originally filed specification. No new matter has been added.

B. October 6, 2009 Examiner Interview

Applicants would like to thank Examiner Yu for the personal interview conducted on October 6, 2009. In compliance with M.P.E.P. § 713.04, the substance of that interview is reflected in the October 6, 2009 Interview Summary and in the following remarks.

In the interview, Applicants' representative proposed amending the claims to include a subtraction analyzer which would differentiate the claims from Litman, which uses a *dividing* analyzer. Applicant's representative further argued that Litman teaches the second immobilized antibody binding a *predetermined* amount of label, and is therefore not the same as or predictably related to the degree of non-specific binding as required by Claim 1. Applicant clarified that the endogenous or exogenous protein is not the target analyte or the labeled antibody bound to the first immunosensor because the second immunosensor must generate a signal that is predictably related to the degree of non-specific binding. If the labeled antibody is specifically bound to the second immunosensor in a predetermined amount, it cannot be related to the degree of non-specific binding on the first immunosensor, which is required by pending Claim 1.

C. Rejections Under 35 USC §103(a)

Claims 1, 2, 5, 6, 9, 12, 69, 70, and 71 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 6,670,115 ("Zhang") in view of U.S. Patent No. 5,156,953 ("Litman"), for the reasons provided at pages 2-6 of the Office Action. Claims 7 and 10 stand rejected under 35 U.S.C. § 103(a) as allegedly

being unpatentable over Zhang in view of Litman and further in view of U.S. Patent Application Publication No. US 2003/0207330 ("Wescott"), for the reasons provided at pages 6 and 7 of the Office Action. Claim 11 stands rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Zhang in view of Litman and further in view of U.S. Patent Application Publication No. US 2002/0155476 ("Pourmand"). Applicants traverse these rejections, particularly in view of amended Claim 1.

1. The claimed invention.

The invention of independent Claim 1 is an immunosensor system with reduced interference. The system comprises a first immunosensor that includes a first immobilized antibody and generates a first signal based on a sandwich between the first immobilized antibody, a target analyte and a labeled antibody, wherein a portion of the first signal arises from a degree of non-specific binding of the labeled antibody. The system also comprises a second immunosensor that includes a second immobilized antibody and acts as an immuno-reference sensor and generates a second signal that is the same as or predictably related to the degree of non-specific binding, and has an immunocomplex between the second immobilized antibody and an endogenous or exogenous protein that is in a sample and that is not the target analyte. The system further includes a subtraction analyzer configured to determine a corrected signal from the first and second signals.

2. Litman fails to teach or suggest: (a) an immuno-reference sensor that generates a second signal that is the same as or predictably related to the degree of non-specific binding; and (b) a subtraction analyzer.

In the outstanding Office Action, Litman is relied upon, *inter alia*, for allegedly teaching a second immunosensor that includes a second immobilized antibody and acts as an immuno-reference sensor that generates a second signal that is predictably related to the degree of non-specific binding on the first immunosensor. (Office Action at p. 4.) Applicants respectfully disagree and submit that Litman does not teach this feature of the claimed invention.

Litman is directed to an assay method and compositions for determining the presence of an analyte in a sample. Litman discloses the use of a measurement first

surface where the amount of labeled mip which binds to the first surface as a result of mip complex formation is related to the amount of analyte in the assay medium. Litman also discloses the use of a calibration second surface which provides a signal level from the signal generating compound as a result of at least one ligand-receptor binding. (Litman, Col. 2, lines 2-26.) According to Litman, by comparison of the level of signal generating compound at each surface, one can determine whether the amount of analyte is greater or less than a **predetermined amount**, which amount is indicated by the signal generated from the calibration surface. (Litman, Col. 3, lines 9-13 (emphasis added).) Litman further indicates that one can obtain a quantitative determination by *dividing* the signal level at the measurement surface by the signal level on the calibration surface. (Id. at Col. 12, lines 12-15.)

Thus, Litman is directed to a positive control calibration method, in which the measurement signal is divided by a control signal to arrive at a calibrated signal. Unlike present Claim 1, Litman is not trying to assess the degree of non-specific binding of the signal antibody. Instead, Litman *intentionally* seeks specific (antibody mediated) binding on the calibration surface. (See, e.g., Litman Claims 14 and 15, which specifically refer to using an antibody to the catalyst (an anticatalyst) on the calibration surface).

For the Litman positive control calibration method to function correctly, the control signal **must be predetermined** and, as a result, the control signal is <u>not</u> "predictably related to the degree of non-specific binding on the first immunosensor" as required by the presently claimed invention. For this reason, Applicants assert that Litman fails to teach this feature of the claimed invention, and the rejection of Claim 1 under 35 USC §103 should be withdrawn.

In addition, as indicated above, the invention of Claim 1 includes a subtraction analyzer "configured to determine a corrected signal from the first and second signals." As discussed in the present specification, the subtraction analyzer corrects the first

signal through a **subtraction operation** using the second signal.[1] In contrast, since Litman is directed to a positive control calibration method, as indicated above, Litman discloses **dividing** the signal level at the measurement surface by the signal level on the calibration surface. (Litman at Col. 12, lines 12-15.) Thus, Litman also fails to teach the subtraction analyzer feature of the claimed invention, and for this reason also, the rejection of Claim 1 under 35 USC §103 should be withdrawn.

For at least the reasons discussed above, Applicants submit that independent Claim 1 is allowable over the references of record. Because each of Claims 2, 5-7, 9, 10-12 and 69-71 depends from Claim 1, Applicants submit that each of these claims also is in condition for allowance.

D. Conclusion

In view of the above amendments and remarks, it is believed that this application is now in condition for allowance, and a Notice thereof is respectfully requested.

Applicants' attorney may be reached in our Washington, D.C. office by telephone at (202) 625-3633. All correspondence should continue to be directed to our address given below.

Respectfully submitted,

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[1] The second signal optionally may be modified prior to the subtraction operation, for example, to account for any proportionality difference (e.g., due to sensor size difference), any offset, or any other essentially constant difference between the two sensors. (See, e.g., paragraph [0093] of the subject application.)